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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/833,745	04/13/2001	Joseph Roberts	78728/106	2894

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EXAMINER
PATTERSON, CHARLES L JR

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 08/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/833,745	ROBERTS ET AL.	
	Examiner	Art Unit	
	Charles L. Patterson, Jr.	1652	

-- The MAILING DATE of this communication appears on the cover sh t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20 and 24-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20 and 24-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

After consideration of applicants' remarks regarding the restriction requirement, the examiner will examine Groups I-VII. Since claims 21-23 have been cancelled and new claims 24-27 have been added, the examiner will examine claims 1-20 and 24-27.

The disclosure is objected to because of the following informalities:

The new copies of Figures 5, 6 and 13-15 are approved as to the changes in red. However applicants failed to change Figure 8, which is noted in the PTO-948 of 11/1/02. The figure submitted is simply a black box when it is apparently supposed to be a graph of activity vs. pH.

In Table 1, "coordinates" apparently is meant to refer to the residue positions. This is not understood as e.g. SEQ ID NO:13 and 14 have 30 and 24 residues but the "coordinates" in Table 1 are 838-867 and 1370-1393, respectively. Similarly the "coordinates" and residues for the other sequences in Table 1 are not understood. This objection is repeated from the previous action because it was not addressed.

In paragraph 146, line 4, it is stated that "below is a graph". No graph is seen below. This objection is repeated from the previous action because it was not addressed.

Appropriate correction is required.

Claims 4-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4 and 5 are confusing and apparently incorrect in the recitation of "30,000 to 70,000 daltons" and "56,000 daltons", respectively. Applicants argue that support for the 56,000 daltons in claim 5 is found in paragraph 56

and do not state where support for "30,000 to 70,000" is found. That paragraph states that "a polypeptide can have a monomeric molecular weight between about 30,000 and 67,000 daltons…[or] between about 45,000 and 60,000 daltons…[or] about 56,000 daltons". However, the claims are limited to polypeptides having enzymatic activity and according to the second sentence in paragraph 132, the 511 amino acid sequence of SEQ ID NO:10 is "approximately 55 kDa" and that is apparently the only polypeptide disclosed as having enzymatic activity.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 24 and 26-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. It has been decided in light of applicants amendment and arguments to drop the previous 35 USC § 101 rejection and the written description portion of this rejection and do this enablement rejection.

The specification teaches in paragraph 132 that the gene for the histidine ammonia lyase from the family *Corynebacteriaceae* is SEQ ID NO:12 and that the corresponding protein is SEQ ID NO:10. The claims are now drawn to a polypeptide that has enzymatic activity that "is not decreased in the presence of a histidine analog". Applicants argue that the previous rejection

stated that the claims should have recited histidinol and *Corynebacteriaceae* and that this has been done. In arguing the previous 35 USC § 101 rejection applicants argue that "within the present invention, moreover, are molecules that do not contain the active site", quoting paragraph 49, and that "[n]umerous examples of fragments that encompass the active site are given, such as SEQ ID NO:1-5". The claims require polypeptides with enzymatic activity so that apparently "molecules that do not contain the active site" do not fall within this claim limitation. Apparently nowhere is the relationship between SEQ ID NO:1-6 and SEQ ID NO:10 shown. If this has been shown, applicants should point this out. SEQ ID NO:1-4 are shorter than SEQ ID NO:10, while SEQ ID NO:5 is slightly longer. SEQ ID NO:6 contains many Xaa residues, which can be any amino acid at all. The molecular weight of the only enzymatically active polypeptide is apparently 55 kDa (paragraph 132).

Furthermore, claim 1 now state that "the isolated polypeptide may comprise conservative substitutions". A change of even one amino acid may effect the enzymatic activity of an enzyme and the specification does not enable such conservative substitutions in the *Corynebacteriaceae* enzyme. Therefore, it is maintained that the applicants have not taught one skilled in the art to make and/or use the invention of the instant claims.

Claims 7-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention and in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is a combination written description and enablement

rejection. This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection.

Applicant argue that "[t]he claims have been amended to recite an isolated polypeptide having about 40 IU/mg protein of histidine ammonia lyase activity, wherein the histidine ammonia lyase activity is not decreased in the presence of L-histidinol or a therapeutic salt thereof and the isolated polypeptide corresponds in sequence to histidine ammonium lyase of *Corynebacteriaceae* or to a fragment thereof which includes the active site, wherein the isolated polypeptide may comprise conservative substitutions relative to the sequence of histidine ammonia lyase of *Corynebacteriaceae*". This is not agreed with. Independent claims 7 and 16 have not been amended at all and claims 8 and 12 do not have the limitation of "about 40 IU/mg protein". Also, the addition of "the polypeptide may comprise conservative substitutions" has been made to claims 8 and 12. A change of even one amino acid may effect the enzymatic activity of an enzyme and the specification does not enable such conservative substitutions in the *Corynebacteriaceae* enzyme.

Applicants further argue that three cited reference teach that t-UA can be isomerized to C-UA at 310 nm, that c-UA plays a role in UVB-induced immunosuppressive mediators and that this property can be used, for example, to treat immune system disorders and to prevent rejection of transplanted organs. One of ordinary skill in the art would not believe that these combinations of theoretical teachings show that the embodiments of claims 16-20 will deliver an immunosuppressant to a patient. The specification does not show that administering histidine ammonium lyase to a patient and then subjecting the patient to an irradiating agent will deliver a immunosuppressant to the patient. Exactly what occurs in a patient cannot be predicted from combining

several theoretical things and presuming it will occur in the patient, absent some convincing proof to the contrary.

It is maintained that one of ordinary skill in the art would not believe that applicants had possession of the claimed invention when the application was filed and also would not be taught by the instant specification how to make and/or use invention within the scope of the instant claims.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5 and 24-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Roberts, et al. (A1). This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection.

Applicants argue that the instant reference does not teach purified HAL, citing a specific activity of 2.1 IU/mg vs. 40 IU/mg for the polypeptide of the instant invention. This characterization is not agreed with. The enzyme taught by the reference <u>is</u> "purified", just not to the extent of the

polypeptide of the instant invention. The sequencing of a protein does not lend any patentability to the protein *per se*. It is maintained that the enzyme taught by the instant reference is the same as in the instant claims, absent convincing proof to the contrary. If applicant later adds some level of purity to the instant claims, then references teaching purification of a protein might be added to the instant rejection.

Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Roberts, et al (A1) in view of either of Shittigar (A) or Kinstler, et al. (B). This rejection is repeated for the reasons given in the last action. Applicants arguments have been carefully considered but do not overcome the instant rejection. Applicants rely on the argument that the primary reference does not teach the enzyme and do not further argue this rejection. Therefore the rejection is repeated.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the

advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charles L. Patterson, Jr., PhD, whose telephone number is 703-308-1834. The examiner can normally be reached on Monday - Friday, 7:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone number is 703-308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Charles L. Patterson, Jr.
Primary Examiner
Art Unit 1652

Patterson
August 15, 2003